REMARKS

Interview

The undersigned appreciates the time the Examiner took to have an interview concerning this application and appreciates the suggestions made by the Examiner during the interview.

Rejections Under 35 U.S.C. § 103

Claims 1-4 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Sechler et al. in view of Wydner et al. Claims 1-4 are drawn to a mouse or mouse cell comprising i) exactly one functional elastin gene and either an elastin gene comprising a null mutation or no second elastin gene, or ii) a mouse or mouse cell comprising no elastin gene or comprising an elastin gene comprising a null mutation and comprising no wild-type elastin gene. In brief, the rejection is that the Sechler et al. reference teaches making transgenic mice which are +/- or -/- for a rat tropoelastin gene. The Wydner et al. reference teaches the sequence of the mouse elastin gene.

Applicants urge that at best the combination of the cited references would motivate one of skill in the art to make mice which are transgenic for a mutated mouse elastin gene but which also comprise normal wild-type mouse elastin genes. The mice of the Sechler et al. reference comprise not only the transgenic mutant rat elastin gene but also comprise the normal wild-type mouse elastin genes which are still active. This is seen in several places in the reference. The first paragraph of the Results and discussion section on page 150 of the Sechler et al. reference states that the reasoning behind the construction of the mice was to produce mice which would synthesize a mutated elastin which would be incorporated into the elastin matrix together with the normal, endogenous mouse elastin. This clearly establishes the motivation of producing the mice - to study animals making a combination of both mutant and wild-type elastin. Data showing that the mice studied for the publication did in fact produce both types of elastin is shown, e.g., in Table 1 on page 153 of the Sechler et al. publication. Both rat and mouse tropoelastin mRNA were produced with the levels of endogenous mouse tropoelastin mRNA set at a value of 100% and the rat levels based on a comparison to that value. The middle of the last paragraph on page 14 of the publication states that levels of expression of the rat transgenes in skin was usually comparable to or exceeded that of the

endogenous expression of the mouse gene. Table 2 on page 158 of the Sechler et al. publication shows that both the rat and mouse elastin proteins were being synthesized in the transgenic animals.

The claims which are pending are not drawn to mice or mouse cells comprising a mutated gene plus a wild-type gene, rather the claims are drawn to mice or cells which have a) a single functional elastin gene plus b) either i) a second elastin gene which has a null mutation or ii) no second elastin gene. This difference is critical. The claimed mice and cells are ones which end up being deficient in elastin rather than comprising some type of mutated elastin. Mice (and humans) which are deficient in elastin have different medical conditions than those which synthesize a mutated elastin.

Claims 1-4 have been amended to state that the "nonfunctional elastin gene" as it had previously been referred to means a gene which comprises a null mutation. The "nonfunctional" language is no longer present in the claim, but the requirement for a null mutation is now present in those cases in which a second elastin gene is present. The amended claims therefore do not encompass elastin genes which are transcribed but are nonfunctional because of a mutation which is present, rather they encompass the presence of only at most a single elastin gene which produces an elastin protein which can be incorporated into a matrix. Support for a "null mutation" is found throughout the application, e.g., page 2, lines 17-18, and on page 5, lines 9-24. It is urged that this amended claim language more clearly distinguishes the claims from the prior art and prevents the claims from being read broadly enough to be encompassed by or made obvious by the prior art. No prior art reference has been cited which teaches a mouse or mouse cell which comprises zero or only one elastin gene which will be transcribed into RNA which will be translated into a protein which can be incorporated into the extracellular matrix.

Claims 5, 6, 9 and 10 were rejected as being unpatentable over Reitamo et al. in view of Sechler et al. and Wydner et al. These claims are drawn to methods for screening for drug candidates useful for treating humans with SVAS, hypertension or atherosclerosis.

First it is urged that claim 6 was improperly included in this rejection. In the first Office Action which was mailed 2 February 2000, claim 6 was rejected under 35 U.S.C. § 103(a) as being

unpatentable over Maruyama et al. in view of Sechler whereas claims 5, 9 and 10 were rejected as being unpatentable over Reitamo et al. in view of Li et al., Su et al. and Li et al. Claim 6 differs from claim 5, 9 and 10 in that it concerns a method of measuring elastase activity whereas the other claims are not concerned with elastase activity. It was the Maruyama et al. reference which was cited for its teaching of elastase. The presently cited Reitamo et al., Sechler et al. and Wydner et al. references do not include a teaching of elastase and it is urged that they cannot make obvious a method which requires the use of elastase.

Claims 5, 9 and 10 are hereby amended to refer to mice or humans or their cells which are *ELN* +/- with the further requirement that these organisms or cells comprise only one functional elastin gene and either no second elastin gene or an elastin gene with a null mutation. It is urged that these amendments prevent the claims from being read to encompass the use of organisms or cells which comprise one wild-type elastin gene plus one mutated elastin gene wherein the mutated elastin gene results in the synthesis of a mutated elastin which can be incorporated into extracellular matrix. It is urged that the cited prior art neither teaches nor suggests a mouse or human with only a single elastin gene which produces elastin which will be incorporated into extracellular matrix or using such organisms or cells for drug screening for drugs which will be useful for treating atherosclerosis, SVAS or hypertension.

In view of the amendments and above arguments, it is requested that the rejections under 35 U.S.C. § 103(a) be withdrawn.

In view of the amendments and above arguments, it is submitted that the present claims satisfy the provisions of the patent statutes and are patentable over the prior art. Reconsideration of this application and early notice of allowance are requested. The Examiner is invited to telephone the undersigned to expedite allowance of this application. If any further extensions of time are

required, the Examiner is authorized to charge such extension of time to our deposit account number 02-2135.

RESPECTFULLY SUBMITTED,					
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Attachments: Marked-Up Copy of Amendments to Claims 1-5 and 9-10.

Amended Claims: Version with markings to show changes made

1 (three times amended). A mouse comprising a genome comprising a) exactly one functional elastin gene and b) either one [nonfunctional] mouse elastin gene comprising a null mutation or no second elastin gene.

2 (amended). A mouse comprising i) a genome with no [functional] elastin gene or ii) a genome with a) an elastin gene comprising a null mutation and b) no functional elastin gene.

3 (three times amended). A mouse cell comprising a genome comprising a) exactly one functional elastin gene and b) one [nonfunctional] mouse elastin gene comprising a null mutation or no second elastin gene.

4 (amended). A mouse cell comprising i) a genome with no [functional] elastin gene or ii) a genome with a) an elastin gene comprising a null mutation and b) no functional elastin gene.

5 (twice amended). A method to screen for drug candidates useful for treating humans with SVAS, hypertension or atherosclerosis or useful for preventing atherosclerosis in humans, said method comprising administering said drugs to an *ELN* +/- mouse or human, wherein said *ELN* +/- mouse or human comprises a genome with a) exactly one functional elastin gene and b) either one elastin gene comprising a null mutation or no second elastin gene, wherein drugs which inhibit occlusion of arteries in said organism are said drug candidates.

9 (twice amended). A method to screen for a drug candidate useful for treating atherosclerosis, hypertension or SVAS in a human, said method comprising treating an *ELN* +/- mouse or human or *ELN* +/- mouse or human cells, wherein said *ELN* +/- mouse or human or mouse or human cells comprise a genome with a) exactly one functional elastin gene and b) either one elastin gene comprising a null mutation or no second elastin gene, with drugs and measuring

synthesis of elastin RNA wherein a drug which increases synthesis of elastin RNA in said organisms or in said cells is said drug candidate.

10 (amended). A method to screen for a drug candidate useful for treating atherosclerosis, hypertension or SVAS in a human, said method comprising treating *ELN* +/- mice or *ELN* +/- mouse cells, wherein said *ELN* +/- mice or mouse cells comprise a genome with a) exactly one functional elastin gene and b) either one elastin gene comprising a null mutation or no second elastin gene, with drugs and measuring synthesis of elastin wherein a drug which increases synthesis of elastin is said drug candidate.